REMARKS

The office action of July 7, 2009 has been carefully reviewed. Claims 1-5, 11, 16-23, 25-69 are pending. Claim 57 has been amended.

DOUBLE-PATENTING

The Examiner has provisionally rejected instant claims 1-5, 11, 16-23 and 25-69 on the ground of nonstatutory double-patenting over claims 1-24 of U.S. Patent 7,288,768 (the '768 patent), contending that the subject matter claimed in the instant application is not patentably distinct from the '768 patent. Without acquiescing in the Examiner's double-patenting rejection, Applicants have transmitted herewith a Terminal Disclaimer under 37 C.F.R. 1.321 disclaiming the portion of any patent granted on the present application which would extend beyond the expiration date of the full statutory term of U.S. Patent No. 7,288,768. Withdrawal of the obviousness-type double patenting rejection of claims 1-5, 11, 16-23 and 25-69 is respectfully requested.

CLAIM REJECTIONS BASED ON §112, FIRST PARAGRAPH

The Examiner rejected claims 1, 3-5, 11, 16-17, 19-23 and 25-27 under 35 U.S.C. §112, first paragraph alleging that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner has alleged, "[t]he Applicants did not reasonable convey to a [sic] skilled in the art that they possessed the invention in the full scope of the claims at the time when the application was filed by 'describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.' The claims recite a method of measuring *an amount of organic substance* [sic] contained within a biological sample, while the whole disclosure is directed toward the method of detecting *glucose* level in the biological sample, with no other organic compounds disclosed in the specification as being measured by the claimed method."

The Examiner referred to MPEP 2163.02 which primarily addresses a lack of written description due to amendments to the claims which introduced new matter. Applicants refer the Examiner to MPEP 2163.03 which states, "[w]hile a question as to whether a

specification provides an adequate written description may arise in the context of an original claim which is not described sufficiently, hereinafter the Lilly doctrine (see, e.g.,*Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997)), there is a ***strong presumption*** that an adequate written description of the claimed invention is present in the specification as filed. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). Consequently, rejection of an original claim for lack of written description ***should be rare***." (emphasis added)

First, Applicants point out that the term "organic substance" is used throughout the specification. Illustratively, the term can be found in paragraphs [0002], [0015], [0017], [0018], [0019], [0020], [0021], [0070], [0071], [0073], [0074], [0075], [0076], [0077], [0078], [0079], [0080], [0081], [0082], [0084], [0085], [0092], [0093], [00100], [00102], [00104], [00105], and [00179]. Furthermore, the term was used in independent claims 1, 23, 24, and 27, as originally filed. The *in haec verba* antecendence of this term is clearly satisfied. The express use of this term throughout the specification and in the claims at the time of the filing reasonably conveys to the artisan that the inventor had possession at that time of the claimed subject matter.

Since the term in question is supported expressly by the specification, Applicants assume that Examiner is rejecting the term under the Lilly doctrine. The Lilly doctrine states that "possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention." *Regents v. Eli Lilly,* 1568.

First, Applicants submit that a method of measuring an amount of an organic substance was possessed at the time of the invention because an actual reduction to practice is described. Applicants point out that the specification includes descriptions of experiments actually performed in determining the amount of glucose in a biological sample. Glucose is an organic substance, accordingly, the example is an actual reduction to practice. Second, the specification goes to great length to describe how the glucose example can be generalized for other organic substances. For example, one would only have to follow the process of obtaining an organic spectra and selecting the appropriate wavelengths for an analysis identical to that as described for glucose, these steps are described in paragraphs [0076] through [0078], included here for the Examiner's convenience.

[0076] To provide a measurement of the amount (e.g., the concentration) of an organic substance contained within a biological sample, the biological sample is illuminated with electromagnetic radiation, such as infrared electromagnetic radiation. For example, a beam of incoherent infrared electromagnetic radiation can be passed through a biological fluid, such as capillary filtrate fluid, so that the organic substance of interest contained within the biological fluid influences the electromagnetic radiation. Preferably, the organic substance contained within the biological fluid absorbs the electromagnetic radiation so as to create an absorption spectrum which, as discussed above, includes a set (n) of wavelength regions where each of the wavelength regions substantially correspond to an absorption band of the absorption spectrum. After illuminating the biological sample with the electromagnetic radiation, the intensity (e.g., detecting the transmittance) of the wavelength bands and reference wavelength bands are detected with a detection system. In particular, it should be understood that the intensity of only the wavelength bands and the reference bands are detected with the detection system. Furthermore, it should be understood that not all of the wavelength bands and reference wavelength bands are detected. In particular, only a select number of wavelength bands of the absorption spectrum are detected along with only a select number of reference wavelength bands. Therefore, it should be appreciated that only the selected wavelength bands and reference wavelength bands are detected with the detection system while the rest of the electromagnetic radiation is substantially prevented from being detected by the detection system. For example, the electromagnetic radiation not included in the selected wavelength bands and reference wavelength bands can be substantially filtered out prior to reaching the detection system. In other words, the detection of the wavelength bands and reference wavelength bands is restricted to a select number of wavelength bands of electromagnetic radiation and a select number of reference wavelength bands of electromagnetic radiation. In particular, the number of selected wavelength bands of electromagnetic radiation is equal to n-1 or less. That is, the number of selected wavelength bands of electromagnetic radiation is a subset of (n).

[0077] With respect to which particular wavelength band, or combination of wavelength bands, is/are selected for detection is dependent upon which wavelength band(s), in combination with the selected reference wavelength band(s), yields spectral data for processing with a mathematical model so as to provide a useful measurement of the amount of organic substance contained within the biological sample. What is meant

herein by "useful" measurement is that the measurement of the amount of organic substance contained with the biological sample is accurate and/or precise enough such that it would be acceptable to utilize in a particular measurement, assay, or application. For example, if a method described herein is utilized in providing a measurement of the amount of glucose contained within capillary filtrate fluid of a diabetic patient, the wavelength bands) and reference wavelength bands) must be selected so that the spectral data supplied to the mathematical model from the combination of these bands results in a glucose measurement that is accurate and/or precise enough such that it informs the patient as to his or her glucose levels within acceptable limits.

[0078] Factors to consider when selecting which wavelength bands) to detect include for example (i) ensuring that the absorption band contained within the wavelength band is, or includes, an absorption band of the organic substance of interest, (ii) selecting a wavelength band which has relatively strong absorption, and (iii) selecting a wavelength band where the strength of the wavelength band correlates well with the amount of organic substance of interest contained in the biological sample. In addition, it is preferable that the selected wavelength bands) is relatively free of interference from absorption bands caused by substances other than the organic substance of interest present in the sample (e.g., the selected wavelength band is separated from the wavelength band of the potentially interfering substance). However, it should be understood that in order to utilize the methods described herein, the selected wavelength bands) does not have to be free of interfering absorption bands caused by substances other than the organic substance of interest. Accordingly, a selected wavelength bands) may be relatively free of interference from absorption bands caused by substances other than the organic substance of interest, or the selected wavelength bands) may include interfering absorption bands caused by substances other than the organic substance of interest. Therefore, it should be appreciated that the selected wavelength bands) can (i) be relatively free of interference from absorption bands caused by substances other than the organic substance of interest present in the sample, (ii) include interfering absorption bands caused by substances other than the organic substance of interest present in the sample, or (iii) be a combination of selected wavelength bands in which some are relatively free of interference from absorption bands caused by substances other than the organic substance of interest while others include interfering absorption bands caused by substances other than the organic substance of interest.

Second, the specification describes distinguishing identifying characteristics for this method. For, example, one step is transmitting incoherent infrared radiation through a sample. The type and source of this incoherent infrared radiation is described, for example, in paragraph [00132]. The infrared detector as used in the step of detecting the intensity of the transmitted radiation is described in great detail in, for example, paragraph [00100]. Furthermore, an embodiment for carrying out these steps is shown in Fig. 5D.

Accordingly, the Applicants were in possession of a method of measuring an amount of an organic substance contained within a biological sample utilizing a detection system at the time of the invention. Accordingly, the rejection is improper and reconsideration is respectfully requested.

CLAIM REJECTIONS BASED ON §112, SECOND PARAGRAPH

The Examiner rejected claims 1-5, 11, 16-23 and 25-69 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim subject matter which Applicants regard as the invention.

The Examiner has stated, "[t]he examiner did not find any indication in the instant disclosure which would indicate the sources of incoherent radiation." Applicants respectfully direct the Examiner to paragraph [00132]. Applicants have included this below for the Examiner's convenience.

> **[00132]** Emitter 515 may be any of a wide variety of commercially available infrared emitters capable of generating and transmitting radiation in the bandwidths of interest described above. The inventors have used the pulsIR® family of infrared emitters (model number NL8LNC) made by Ion Optics, Inc., of Waltham, MA. These types of emitters are broadband infrared sources that generate signals in the 2-20 μm range.

In paragraph [00132], the disclosure includes an exemplary incoherent radiation source. The emitter is *broadband* and generates signals in the 2-20 μm *range*; accordingly, it is necessarily a source of incoherent radiation. One of ordinary skill in the art would appreciate that phase incoherence is required if a source is generating broadband radiation or generating a *range* of wavelengths. Applicants point out that this is only one of the many locations in the specification describing the incident signal as having a *range* of wavelengths. Similarly, the

manner in which Applicants have used the term incoherent is within its plain and ordinary meaning within the field. One of ordinary skill in the art would not find the use of the term incoherent, according to its ordinary plain meaning, unclear within the claims. Accordingly, Applicants request that the rejection be reconsidered.

Regarding Claim 28, Applicants refer the Examiner to MPEP 2173.04, which states "[b]readth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph." The MPEP further states, "[i]f the claim is too broad because it does not set forth that which applicants regard as their invention as evidenced by statements outside of the application as filed, a rejection under 35 U.S.C. 112, second paragraph, would be appropriate." The Examiner has not pointed to statements outside of the application as filed evidencing the claim is too broad, therefore, the rejection is improper and should be withdrawn.

Applicants have amended Claim 57 to render the Examiner's rejection moot. Applicants submit that no new matter has been added by way of this amendment.

§103 Rejections: Lillenfeld-Toal in view of Krueger

The Examiner rejected claims 1-5, 11, 16-23 and 25 under 35 U.S.C. 103(a) as being unpatentable over Lillenfeld-Toal (US 6,484,044) (Lillenfeld-Toal) in view of Krueger et al., (US 5,365,066) (Krueger), as evidenced by Kim et al., (IEEE Photonics Technology Letters, 2000) (Kim).

Applicants refer to MPEP 2141.02 which states, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)." Applicants submit that Lillenfeld-Toal and Krueger are not combinable because the references teach away from the combination. A combination of references that renders the prior art invention unsatisfactory for its intended purpose is not a satisfactory motivation for combination. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

In a first aspect, Applicants submit that Lillenfeld-Toal teaches away from using an LED infrared source because an LED would render Lillenfeld-Toal's invention inoperable and deviates from the principles upon which the invention was developed. In a second aspect, Applicants submit that Lillenfeld-Toal teaches away from using near infrared radiation, because near infrared radiation could not be used as suggested by the Examiner. Since Krueger uses a LED radiation source emitting near infrared radiation, one of ordinary skill in the art would not attempt to combine the references. One skilled in the art would not combine the elements as suggested because there would be no reasonable expectation of success. The motivation for combination relied upon by the Examiner, to increase measurement sensitivity in LED/IRED near-infrared instruments, is based on a flawed understanding of the Krueger reference.

The Combination is Improper, Reason 1: Lillenfeld-Toal teaches away from a combination with Krueger because Lillenfeld-Toal teaches only mid-infrared radiation and describes why a using near-infrared radiation is not operable.

Applicants direct the Examiner's attention to Lillenfeld-Toal column 2 lines 12-26, which states the following:

> Substances of interest such as glucose have covalent bonds with fundamental resonance frequencies in the *mid-infrared region* of the light spectrum, i.e. at frequencies corresponding to infrared light wavelengths from 2.5 to 25 μm (wavenumbers of 4000 to 400 cm^{-1}). Hence, the mid-infrared region of the absorption spectrum of these substances contains relatively narrow absorption lines specific to each individual substance. *This is an advantage over the use of the near infrared region* at wavelengths from 0.76 to 2.5 μm where infrared absorption by the substances of interest is due to harmonics of the oscillating molecular bonds and absorption bands are broader, overlap each other, have smaller and wider peaks and it is thus more difficult to attribute absorption to the substance to be detected. (emphasis added)

Applicants point out that Lillenfeld-Toal teaches that using near infrared light is a disadvantage making it more difficult to attribute absorption to the substance detected. Therefore, one of ordinary skill in the art would not modify Lillenfeld-Toal to use a near infrared radiation source when such source is expressly described as a disadvantage. Applicants note that Krueger is directed only towards near infrared LEDs. For example, see title, abstract, and entire disclosure. According to Lillenfeld-Toal, using the near infrared LEDs of Krueger would result

in broader and overlapping absorption bands, havin smaller and wider peaks, making it impractical to resolve the analyte from interfering compounds.

Combination is Improper, Reason 2: Lillenfeld-Toal teaches away from a combination with Krueger because Lillenfeld-Toal teaches using a laser and not an LED and describes why a using an LED is not operable.

Applicants point out that Lillenfeld-Toal overcame the challenges of using mid-infrared radiation by using a laser. One of ordinary skill in the art would appreciate that a laser can be thought of as emitting a single wavelength. Lillenfeld-Toal states, "the embodiment measures light absorption photoacoustically with laser light at a plurality of discrete individual wavelengths where the largest photoacoustic effect on the glucose concentration is expected." [column 5, lines 45-48]. To practice the disclosure of Lillenfeld-Toal, a laser is required. The near infrared LED of Krueger is not a laser and would not be a suitable replacement for the laser disclosed by Lillenfeld-Toal, because the LED emission bandwidth is much broader than a laser. As Lillenfeld-Toal states, "the use of discrete wavelengths allows sufficient laser beam power concentrated to these wavelengths while avoiding unnecessary heating of the body tissue through irradiation with other less favorable wavelengths." [column 5, lines 51-54]. Accordingly, using the near infrared LEDs of Krueger would result in unnecessary heating of the body tissue and insufficient incident beam powers.

Combination is Improper, Reason 3: One skilled in the art would not combine the elements as suggested because there would be no reasonable expectation of success. The motivation for combination relied upon by the Examiner, to increase measurement sensitivity in LED/IRED near-infrared instruments, would not be realized as suggested by the Examiner.

A careful reading of Krueger reveals that the LED radiation source could not be implemented in the design of Lillenfeld-Toal to increase measurement sensitivity as suggested by the Examiner.

The disclosure of Krueger describes using the near infrared LEDs to transmit light through a finger. Figure 2 of Krueger clearly shows this fact. In contrast to transmitting through a sample, Lillenfeld-Toal teaches that the photoacoustic effect allows measurement of the light absorbance by glucose *even where virtually no light escapes again from the body tissue under investigation*. It is clear the two inventions are operating based on completely separate principles. The Krueger invention is operating on the principle that the intensity of the near infrared radiation can be increased by using an LED, so that additional light can be transmitted

through a finger. The Lillenfeld-Toal invention is operating on the principle that the mid infrared spectrum can be used through the use of a laser and the photoacoustic effect. Based on Lillenfeld-Toal's disclosure of the reasoning behind using both a laser and the mid infrared region of the spectrum, one of ordinary skill in the art would not modify the invention to include a near infrared LED, it would go against the very reasoning upon which he based his invention. As Lillenfeld-Toal states,

> What was previously believed a disadvantage of noninvasive detection of substances such as glucose in body fluids or tissue by mid infrared spectroscopy, namely *the high parasitic absorption of mid-infrared light by water is overcome by detecting absorption through the photoacoustic effect and by using laser light* at a plurality of discrete wavelengths. [column 2, lines 26-33]

> Measuring the absorbance at discrete wavelengths at maxima or minima of absorption bands means in practice to measure the absorbance of an infrared light *beam having a bandwidth smaller than the width of the corresponding absorption or transmission band.* Preferably, the bandwidth of the light beam should not exceed 2/3 or 1/3 the width of the band of the absorption spectrum where the minimum or maximum is measured.
>
> Hence, the embodiment measures *light absorption photoacoustically with laser light* at a plurality of discrete individual wavelengths where the largest photoacoustic effect on the glucose concentration is expected. And the use of discrete wavelengths allows sufficient laser beam power concentrated to these wavelengths while avoiding unnecessary heating of the body tissue through irradiation with other less favorable wavelengths. The preferred device for emitting the mid-infrared radiation at selected wavelengths, with sufficient intensity but limited overall power so as to avoid overheating of the body tissue is a semiconductor laser having a quantum well structure. [column 5, lines 36-59]

This differs significantly from Krueger whom is only interested in near infrared measurements. For example, Krueger states, "[t]hus, there is a great need for a near-infrared measurement instrument which provides the resolution necessary for precision measurement using near-infrared techniques but without the expensive electronic circuitry currently necessary to achieve high resolution measurements." [column 2, lines 38-42]

For at least these reasons, the Applicants submit that the combination of Lillenfeld-Toal and Krueger is improper and should be withdrawn.

In the Response to Arguments section the Examiner stated, "[t]he examiner did not indicate that Lillenfeld-Toal does not teach transmitting infrared radiation - what else can Lillenfeld-Toal teach, if he teaches detection of glucose with IR spectroscopy?" Applicants will attempt to answer to that question for the Examiner; Lillenfeld-Toal teaches the photoacoustic effect. Applicants refer to U.S. Patent No. 6,348,968, which will be filed in an accompanying information disclosure statement, which states,

> Photoacoustic spectroscopy is an analytical method that involves stimulating a sample by light and subsequently detecting sound waves emanating from the sample. Typically, only a narrow range of wavelengths of light are introduced into a sample. Such narrow range of wavelengths of light can be formed by, for example, a laser. Utilization of only a narrow range of wavelengths can enable preselected molecular transitions to be selectively stimulated and studied.
>
> A photoacoustic signal can occur as follows. First, light stimulates a molecule within a sample. Such stimulation can include, for example, absorption of the light by the molecule to change an energy state of the molecule. Second, an excited state structure of the stimulated molecule rearranges. During such rearrangement, heat, light, volume changes and other forms of energy can dissipate into an environment surrounding the molecule. Such forms of energy cause expansion or contraction of materials within the environment. As the materials expand, sound waves are generated. Accordingly, an acoustic detector mounted in acoustic communication with the environment can detect changes occurring as a result of the light stimulation of the absorbing molecule. [column 1, lines 16-40]

Accordingly, one of ordinary skill in the art would appreciate that Lillenfeld-Toal does not teach transmitting infrared radiation; rather, it relies upon detecting an acoustic signal. The photoacoustic effect does not rely on transmission of infrared radiation; but rather, it relies on the absorption of infrared radiation and the on the propogation of sound waves through the sample.

§103 Rejections: Heise, etc. in view of Sterling

The Examiner rejected claim 26 under 35 U.S.C. 103(a) as being unpatentable over anyone of Heise et a., (Appl. Spectr., 1994) (Heise), Bhandare et al., (Appl. Spectr., 1994) (Bhandare), Budinova et al., (Appl. Spectr., 1997) (Budinova), or Vonach et al., (Appl. Spectr., 1998) (Vonach) in view of Sterling et al., (US 6,025,597, IDS) (Sterling).

As discussed in the previous two responses, Heise, Bhandare, Budinova and Vonach all utilize FTIR (Fourier-Transform Infrared) spectroscopy. Heise (line 3 of the Abstract), Bhandare (paragraph 1 of Experimental), Vonach (line 1, Abstract) and Budinova (paragraph 3, introduction) each disclose the use of FTIR. In pointing this out previously, Applicants also showed how each of the references taught away from using a non-FTIR approach. In response to the previous arguments, the Examiner stated the following in the Response to Arguments,

> [I]t is not apparent, as to what the mathematical transformation of the signals, specifically Fourier-transform, has to do with transmitting infrared radiation'? The examiner did not find anywhere in the claim recitation of the "simple transmittance experiments". Furthermore, Budinova recites the "simple transmittance experiments" in association with attenuated total reflectance (ATR), which is also not recited in claim 26. Moreover, it is not apparent, as to why the Applicants constantly refer to the mid-IR spectrum, which is difficult to measure with FTIR, when no mid-IR is recited in the claim? This renders the Applicants' arguments irrelevant to the recited subject matter and to the rejections established by the examiner.

First, Applicants respectfully point out that claim 26 was amended to include the element of mid infrared radiation in response to the Office Action mailed October 27, 2008.

Second, Applicants point out that one element of claim 26 is filtering the electromagnetic radiation such that only radiation which corresponds to the n wavelength regions reaches the detector. Applicants submit that one of ordinary skill in the art would appreciate that this element requires the method to not include a Fourier transform step. Applicants make reference to the "Introduction to Fourier Transform Infrared Spectrometry" publication, a copy of which is submitted with the accompanying information disclosure statement. The transmitted radiation in a FTIR is an interferogram. All FTIR utilize an interferometer to generate this

interferogram from a infrared source. Applicants point out that page 4 states, "The interferometer produces a unique type of signal which has all of the infrared frequencies 'encoded' into it." Furthermore, page 4 states, "[b]ecause the analyst requires a **frequency spectrum** (a plot of the intensity at each individual frequency) in order to make an identification, the measured interferogram signal can not be interpreted directly." (emphasis in original) Accordingly, Applicants point out that the detector in an FTIR detects an interferogram. Claim 26 requires that only radiation which corresponds to the n wavelength regions reaches detector. An interferogram is not "only radiation which corresponds to n wavelength regions." Rather, it is a type of signal that requires a special detector distinct from the type described in the present application. Applicants refer again to "Introduction to Fourier Transform Infrared Spectrometry," page 5 states that "[t]he detectors used are specially designed to measure the special interferogram signal." Applicants submit that applying a Fourier transform is more than a mathematical data treatment as suggested by the Examiner. Rather, the need to apply a Fourier transform to the data is instigated by the use of an interferogram to probe the sample. In contrast to detecting this interferogram in FTIR, claim 26 includes a step such that only radiation which corresponds to the n wavelength regions reaches the detector.

While FTIR analyses have certain advantages, Applicants have proposed a method entirely distinct from the FTIR approach for reasons that are clear from the specification. Specifically, paragraph [0082] which is provided here for the Examiner's convenience, describes an exemplary reason for avoiding FTIR.

> **[0082]** It should be appreciated that detecting and processing spectral data only from the selected wavelength band(s) and reference wavelength band(s) simplifies the process of providing a useful measurement of the amount of an organic substance of interest contained within a biological sample. For example, since an apparatus for performing a method described herein only detects and processes spectral data from a select number of wavelength bands and reference wavelength bands it is less complex as compared to an apparatus configured to detect and process spectral data from all of the wavelength bands of an absorption spectrum. Accordingly, an apparatus configured to perform one of the methods described herein lends itself to being smaller, compact and portable.

As discussed in the previous two responses, Heise, Bhandare, Budinova and Vonach all utilize FTIR (Fourier-Transform Infrared) spectroscopy and teach away from using a

non-FTIR approach. Specifically, Heise distinguishes FTIR from "simple" transmission spectroscopy by stating, "[t]hese complications can be reduced with the use of near-infrared spectroscopy with simple transmittance experiments, for which cell pathlengths of millimeters are needed, so that the adsorbed layers play an extremely minor part in the absorbances measured." This excerpt, taken from the Conclusions, 2nd paragraph, is contrasting a "simple" transmittance experiment from an experiment utilizing Fourier transform mathematics and interferometer based optics. In this statement, Heise is implying that simple transmittance measurements are impossible with mid infrared radiation, however, near-infrared radiation can be used. Therefore, Heise is teaching away from mid infrared electromagnetic radiation when not used with FTIR.

Similarly Budinova distinguishes a "simple transmittance" measurement from using FTIR. Applicants respectfully refer Examiner to paragraph 2 and 3 of the Introduction on page 631 which is included below for the Examiner's convenience:

> The mid-IR region is useful in the invasive method of blood component determination by the attenuated total reflectance (ATR) technique[1-9] but simple transmittance measurements of liquid blood or blood serum are impossible in the mid-IR because of the presence of water in the matrix. ATR experiments are performed by employing ZnSe crystal-based flow cells; this approach, however, is associated with some shortcomings, such as the adsorption of proteins on the crystal, which requires the cell to be demounted and the crystal to be polished frequently.
>
> In the present work, the ATR technique was avoided; instead, the feasibility was examined of employing Fourier transform infrared (FT-IR) spectroscopy in the mid-IR region for determining glucose and cholesterol in whole blood and blood serum samples trapped on a polyethylene carrier and then dried.

Not only does Budinova teach away from the exact combination the Examiner has alleged is obvious, Budinova explicitly states that simple transmittance measurements of liquid blood or blood serum (i.e. biological sample) is impossible. When reading Heise and Budinova, it is clear that it was generally accepted in the art that FTIR was required when analyzing biological samples with mid infrared radiation.

The disclosure of Bhandare does not teach a method for analyzing a sample containing glucose, but rather, Bhandare merely compares several different techniques for analyzing FTIR spectrum. Applicants submit that analyzing an FTIR spectrum is not an element of the claim 26 and it is not clear why the Examiner has incorporated this reference. Applicants

remind the Examiner of the Supreme Court's requirements for showing obviousness as described in *KSR v. Teleflex*, "[i]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." The Examiner has failed to point to any portion of Bhandare which teaches any element of the claimed method, much less a reason that one of ordinary skill in the art would have combined Bhandare with Sterling as proposed.

Regarding Sterling, the examiner alleges that "Sterling provides direct disclosure for both types of methods, i.e. the method of using FTIR instrument with post-detected processing the signals related to the analyte, e.g. glucose, or method of using spectral filters build-in into the IR spectrometer for the specific analyte, e.g. glucose, which makes the modification of any of the teachings provided above for FTIR analysis of glucose obvious for a person of ordinary skill in the art." First, the Applicants would like to point out that Sterling teaches against using transmission techniques generally (note that each of the FTIR methods cited above is a transmission technique). The entire disclosure is directed at techniques wholly distinct from transmission spectroscopy. Rather, the Sterling reference describes a method which avoids the "severe limitations" of transmission techniques. Sterling states, "[t]he transmission mode technique has severe limitations if the substance being measured is very dense in the wavelength region of interest. For instance if one was analyzing glucose dissolved in water or human blood the 9 to 10 micron wavelength region would be ideal however the incident analysis beam would be totally absorbed with less than 200 microns of path length. Maintaining a sample of such thin proportions is difficult." [column 1, lines 55-62] Rather than teaching a transmission technique, Sterling describes the reasons why such an approach should not be pursued. A person of ordinary skill in the art would not combine Sterling's approach with a transmission technique.

Applicants submit that claim 26 is patentably distinct from the combination of any one of Heise, Bhandare, Budinova, or Vonach in view of Sterling. Accordingly, reconsideration is respectfully requested.

§103 Rejections: Clarke in view of Muller

The Examiner rejected claim 27 under 35 U.S.C. 103(a) as being unpatentable over Clarke (US 5,054,487) in view of e.g. Muller (US 4,427,889).

Applicants point out that the Clarke reference is directed at visible and near infrared radiation, "a multiple wavelength illumination source which provides light at a series of *skin penetrating* wavelengths (e.g. from about 500 nm to about 2000 nm)." [reference numbers omitted, emphasis added, column 3, line 34-37]. In rejecting claim 27, the Examiner simply replaced the near infrared radiation of Clarke with the mid infrared radiation of Muller without consideration as to whether such wavelengths were *skin penetrating*. Because is it well-known that mid infrared does not effectively penetrate skin, Applicants submit that such a combination would render Clarke inoperable. It is well-known in the art that mid infrared radiation does not readily transmit through a water-containing sample (such as skin). Reference is made to Budinova, as previously cited, "simple transmittance measurements of liquid blood or blood serum are impossible in the mid-IR because of the presence of water in the matrix." [page 1, column 1, last paragraph] Further, Lillenfeld-Toal states, "the high parasitic absorption of mid-infrared light by water" [Lillenfeld-Toal, column 2, lines 29-30] creates a situation in which "virtually no light escapes again from the body tissue under investigation." [Lillenfeld-Toal, column 5, line 50] Accordingly, the use of mid infrared in place of the near infrared radiation would result in virtually no light being emitted. The modification suggested by the Examiner renders the Clarke reference inoperable. Accordingly, Applicants request that the Examiner withdraw the rejection of claim 27.

§103 Rejections: Lillenfeld-Toal in view of Krueger, Purdy, Rule, and Sterling

The Examiner rejected claim 28-69 under 35 U.S.C. 103(a) as being unpatentable over combinations which rely on the combination of Lillenfeld-Toal and Krueger.

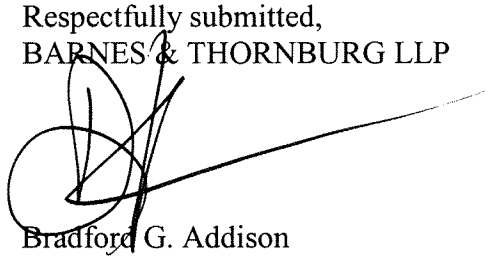
As discussed above, Lillenfeld-Toal and Krueger are not combinable. None of Purdy, Rule, and/or Sterling are cited for nor make up for the deficiency in the combination referred to above with respect to the rejection of claims 1-5, 11, 16-23 and 25. For at least this reason, the combinations do not arrive at the invention recited in the present claims. Reconsideration of the rejection is respectfully requested.

CONCLUSION

Applicant believes that the present application is now in condition for allowance and such action is respectfully requested. If there are any questions or comments that would speed prosecution of this application, the Examiner is invited to call the undersigned at 317-231-7701.

It is respectfully requested that, if necessary to effect a timely response, this paper be considered as a Petition for an Extension of Time sufficient to effect a timely response and that shortages in fees, if any, be charged, or any overpayment in fees credited, to the Account of Barnes & Thornburg, Deposit Account No. 10-0435 with reference to file 3220-73780.

Respectfully submitted,
BARNES & THORNBURG LLP



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